Remarks

Status of the Claims

Claims 30, 31, 33, 35, 37-39, 44-47 and 57-59 have been canceled. Claims 1-3, 5-23, 26, 28, 29, 54 and 55 have been amended. Thus, claims 1-3, 5-23, 26, 28, 29, 54 and 55 remain presented for examination, with claims 1-3 being the independent claims. Support for the amendment to claims 1-3 may be found in the specification at page 21, line 18 to page 22, line 22, and in original claims 44-46; the amendments to the remaining claims are sought to place them into proper dependent format upon amendment of claims 1-3. No new matter is added by these amendments, and their entry and consideration are respectfully requested.

Claim objections

In the Office Action at page 4, claims 33, 35 and 37-39 were objected to as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. Claims 33, 35 and 37-39 have been canceled, thus rendering this rejection moot.

Thus, Applicants respectfully request withdrawal of the claim objections.

Rejection Under 35 U.S.C. § 112, second paragraph

In the Office Action at pages 4-6, claims 1-3, 5-23, 26, 28-31, 33, 35, 37-39, 44-47, 54-55, 57 and 59 were rejected under 35 U.S.C. § 112, second paragraph, as the meaning of the phrase "without dilution" as recited in these claims is alleged to be unclear. By the foregoing amendments, claims 44-47 have been canceled, thus rendering this rejection moot as it may have applied to these claims. Applicants respectfully traverse the rejection as it may be applied to the remaining claims.

Claims 1-3 as amended (and thus, the remaining claims that depend directly or ultimately therefrom) recite "***without dilution prior to said contacting***" (*i.e.*, the composition is not diluted prior to contacting the composition with the nucleic acid molecule to be synthesized, sequenced, or amplified). The meaning is of this phrase is clear on its face, and is made abundantly clear by reference to the present specification. Thus, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. § 102(b)

In the Office Action at pages 6-8, claims 1, 44 and 54 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Scalice *et al.* (U.S. Patent No. 5,338,671). Applicants respectfully traverse this rejection.

Scalice discloses the use of a 2.5X concentrate, not reagents which are present at concentrations for performing methods without dilution as recited in the pending claims. Specifically, Scalice discloses a reaction mixture which initially comprises 2.22 nanomolar *Taq* DNA polymerase and 250 nanomolar antibody to *Taq* polymerase (*see* Scalice at col. 15, lines 47-49). According to Scalice, other components, including nucleic acid molecules, are then added to the composition to initiate polymerization, resulting in a mixture having a *Taq* polymerase concentration of 0.89 nanomolar and an antibody concentration of 100 nanomolar (*see* Scalice at col. 15, line 68, to col. 16, line 1). This mixture disclosed in Scalice thus represents a 2.5X dilution (250/100 = 2.5; 2.22/0.89 = 2.5) of the composition prior to use, in contrast to the compositions used in the presently claimed methods which are not diluted prior to use. Thus, claims 1, 44 and 54 are not anticipated by Scalice, and Applicants

respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

Rejection under 35 U.S.C. § 102(e)

In the Office Action at pages 8-10, claims 1, 2, 5, 26, 28, 30, 33, 54, 55 and 57 were rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Gelfand *et al.* (U.S. Patent No. 5,618,703). Claims 30, 33 and 57 have been canceled, thus obviating the portion of this rejection that may have applied to these claims. Applicants respectfully traverse this rejection as it may be applied to the remaining claims, which recite the use of compositions that comprise at least one antibody that binds to a thermostable DNA polymerase. In contrast to the presently claimed methods, Gelfand does not disclose the use of antibodies that bind to thermostable DNA polymerases. Thus, claims 1, 2, 5, 26, 28, 54 and 55 are not anticipated by this reference, and Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(e).

Rejections under 35 U.S.C. § 103(a)

In the Office Action at pages 10-22, the claims have been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over one or more cited references. Applicants respectfully traverse these rejections in view of the following remarks.

I. Claim 8 was rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Gelfand. Claim 8 is indirectly dependent on claims 2 and 3, which recite the use of compositions that comprise at least one antibody that binds to a thermostable DNA

polymerase. As noted above, Gelfand neither discloses nor suggests the use of antibodies that bind to thermostable DNA polymerases. Thus, claim 8 would not have been obvious in view of this reference. Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 103(a).

II. Claims 1-2, 5, 8-9, 26, 28, 30, 33, 54, 55 and 57 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Olsen *et al.* (WO95/00664) in view of Sobol *et al.* (U.S. Patent No. 5,543,296) and Gelfand. By the foregoing amendments, claims 30, 33 and 57 have been canceled, thus rendering the rejection moot as it may have applied to these claims. Applicants respectfully traverse this rejection as it may be applied to the remaining claims, which recite the use of compositions that comprise at least one antibody that binds to a thermostable DNA polymerase. Olsen neither discloses nor suggests the use of an antibody that binds to a thermostable DNA polymerase. This defect in Olsen is not cured by the disclosures of Sobol or Gelfand, which also do not disclose or suggest the use of an antibody that binds to a thermostable DNA polymerase.

Moreover, in direct contrast to the presently claimed methods which involve the use of reagent mixtures that lack nucleic acid molecules, Olsen discloses the use of compositions that include nucleic acid molecules. Thus, the approach disclosed in Olsen is exactly opposite that of the presently claimed invention; Olsen therefore teaches *away* from the invention as presently claimed, and cannot be used in attempting to establish a *prima facie* case of obviousness.

Establishing *prima facie* obviousness requires not only that the combination of prior art disclosures is possible, but also that the disclosures as combined would have (a) motivated

the skilled artisan to make the combination to arrive at the claimed invention, and (b) suggested to the skilled artisan a reasonable likelihood of success in making and using the claimed invention. *See In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988). Absent a showing of such motivation and suggestion, *prima facie* obviousness is not established. *See In re Fine*, 5 USPQ2d at 1598. Indeed, the Federal Circuit specifically instructed that:

> "There is no suggestion to combine... if a reference teaches away from its combination with another source. . . . A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant . . . [or] if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant."

Tec-Air, Inc. v. Dense Manufacturing Michigan Inc., 192 F.3d 1353 (Fed. Cir. 1999) (citation omitted). The Federal Circuit has further instructed that "references that teach away cannot serve to create a *prima facie* case of obviousness," *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994), and that an "applicant may rebut a prima facie case of obviousness by showing that the prior art teaches away from the claimed invention in any material respect." *In re Geisler*, 116 F.3d 1465, 1469 (Fed. Cir. 1997).

As was the case in *Tec-Air*, Olsen teaches away from the claimed invention; the skilled artisan reading Olsen "would be led in a direction divergent from the path that was taken by the applicant." Olsen clearly teaches away from the claimed invention, and thus, in accord with the Federal Circuit's guidance in *Gurley*, cannot serve to support a *prima facie* case of obviousness of the presently claimed invention.

Because nothing in Olsen, Sobol or Gelfand would have motivated the skilled artisan to combine these references to arrive at the claimed invention, and because Olsen actually teaches away from the claimed invention, a *prima facie* showing of obviousness cannot be properly be maintained. Applicants therefore respectfully request that the Examiner reconsider and withdraw this rejection under 35 U.S.C. § 103(a).

III. Claims 44-47 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Olsen in view of Sobol and Gelfand, and further in view of Scalice. By the foregoing amendments, claims 44-47 have been canceled, rendering this rejection moot.

IV. Claims 1-3, 5, 8, 26, 29-31, 33, 35, 54, 55, 57 and 59 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Soderlund *et al.* (EP 0648280 B1) in view of Sobol and Gelfand. By the foregoing amendments, claims 30, 31, 33, 35, 57 and 59 have been canceled, thus rendering the rejection moot as it may have been applied to these claims. Applicants respectfully traverse this rejection as it may be applied to the remaining claims, which recite the use of compositions that comprise at least one antibody that binds to a thermostable DNA polymerase. Soderlund neither discloses nor suggests the use of an antibody that binds to a thermostable enzyme or to a thermostable DNA polymerase. This defect in the disclosure of Soderlund is not cured by Sobol or Gelfand, neither of which discloses the use of an antibody that binds to a thermostable enzyme or to a thermostable DNA polymerase. Applicants therefore respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 103(a).

V. Claims 1, 2, 5, 8, 9, 26, 28, 30, 33, 37-39, 54, 55 and 57 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Barnes in view of Hoeltke *et al.* (U.S. Patent No. 5,814,502), and further in view of Sobol and Gelfand. By the foregoing amendments, claims 30, 33, 37-39 and 57 have been canceled, thus rendering the rejection moot as it may have been applied to these claims. Applicants respectfully traverse this rejection as it may be applied to the remaining claims, which recite the use of compositions that comprise at least one antibody that binds to a thermostable DNA polymerase. Barnes neither discloses nor suggests the use of an antibody that binds to a thermostable DNA polymerase. This defect in the disclosure of Barnes is not cured by Hoeltke, Sobol or Gelfand, none of which discloses or suggests the use of an antibody that binds to a thermostable DNA polymerase. Applicants therefore respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 103(a).

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated or rendered moot. Applicants therefore respectfully request reconsideration and withdrawal of all presently outstanding objections and rejections.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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